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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/475,470	06/07/95	SAMULSKI R	[illegible]

HM21/0213

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EXAMINER	
NELSON,A	
ART UNIT	**PAPER NUMBER**
1649	

DATE MAILED: 02/13/98

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/475,470	Applicant(s) Richard J. Samulski, et al.
	Examiner Amy Nelson	Group Art Unit 1649

☒ Responsive to communication(s) filed on *Nov 21, 1997* .

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-45* is/are pending in the application.

Of the above, claim(s) *36-38 and 40-45* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-35 and 39* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1649.

Declaration under 37CFR §1.132

2. The Samulski Declaration filed 11/21/97 under 37 CFR §1.132 is defective because it is unsigned. A substitute signed Declaration must be submitted for formal consideration.

Claim Rejections - 35 USC § 112

3. Claims 1-35 and 39 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is maintained for the reasons of record set forth in the last Official action mailed 5/21/97. Applicant's arguments filed 11/21/97 have been fully considered but they are not persuasive.

Applicant argues that the specification discloses methods for making recombinant adeno-associated viral vectors, how to purify human bone marrow progenitors from a patient and how to transduce mammalian cells. Applicant asserts that one of ordinary skill in the art could, based on

the provided teachings, transduce mammalian cells with a recombinant adeno-associated viral vector to affect therapeutic treatment of mammalian diseases or disorders (response p. 3-4). Examiner responds that most of the unpredictability associated with *in vivo* gene therapy methods relates not to making recombinant vectors, purifying human progenitor cells and transducing cells, but rather to how to successfully deliver and target the appropriate cells and achieve appropriate expression levels so as to achieve therapeutic benefit. There are many problems associated with gene therapy methods involving viral vectors, as described in the cited NIH reference. The use of viral vectors is still very much in its infancy and significant guidance is required to practice said methods. In the absence of direct experimental evidence that provides guidance on treatment of a specific condition, undue trial and error experimentation would be required to determine how to deliver the recombinant adeno-associated viral vector to the appropriate target cells so as to affectively remedy a particular disease.

Applicant further argues that the submitted Samulski Declaration provides sufficient evidence to enable the invention. Specifically, the Samulski Declaration teaches, based on primate bone marrow transplant experiments, the successful AAV-mediated expression of a globin transgene in erythroid cells, successful transfer of AAV into bone marrow progenitor cells for up to three months, no adverse affects on reconstitution of the transplanted animals, and expression of a functional protein (from the neo^r transgene) (response p. 4-5). Applicant responds that although Applicant teaches successful transduction and expression of a transgene in transplanted cells, Applicant has still provided no guidance with respect to treatment of a specific condition.

Applicant has listed a variety of conditions and the genetic basis for those diseases. However, Applicant has provided no guidance for how to alleviate the symptoms associated with any condition. Applicant's guidance with respect to achieving detectable expression of the introduced transgene does not provide sufficient evidence to indicate that suitable expression, both in magnitude and in cellular/intracellular location, could be achieved with a transgene related to a specific condition, nor that suitable expression of said transgene would result in mediation of disease symptoms. In the absence of specific guidance regarding treatment of a specific condition by the claimed methods, undue trial and error experimentation would be required to practice the invention. Therefore, the invention is not enabled.

Conclusion

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

This application is subject to the provisions of Public Law 103-465, effective June 8, 1995. Accordingly, since this application has been pending for at least two years as of June 8, 1995, taking into account any reference to an earlier filed application under 35 U.S.C. 120, 121 or 365(c), applicant, under 37 CFR 1.129(a), is entitled to have a first submission entered and considered on the merits if, prior to abandonment, the submission and the fee set forth in 37 CFR 1.17(r) are filed prior to the filing of an appeal brief under 37 CFR 1.192. Upon the timely filing of a first submission and the appropriate fee of $790.00 for a large entity under 37 CFR 1.17(r), the finality of the previous Office action will be withdrawn. If a notice of appeal and the appeal fee set forth in 37 CFR 1.17(e) were filed prior to or with the payment of the fee set forth in 37 CFR 1.17(r), the payment of the fee set forth in 37 CFR 1.17(r) by applicant will be construed as a request to dismiss the appeal and to continue prosecution under 37 CFR 1.129(a). In view of 35 U.S.C. 132, no amendment considered as a result of payment of the fee set forth in 37 CFR 1.17(r) may introduce new matter into the disclosure of the application.

If applicant has filed multiple proposed amendments which, when entered, would conflict with one another, specific instructions for entry or non-entry of each such amendment should be provided upon payment of any fee under 37 CFR 1.17(r).

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy J. Nelson whose telephone number is (703) 306-3218. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Douglas Robinson, can be reached at (703) 308-2897. The fax phone number for this Group is (703) 308-4242 or (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

DAVID T. FOX
PRIMARY EXAMINER
GROUP ~~180~~ 1649

Amy J. Nelson, Ph.D.

February 11, 1998